STUDIES ON HEADACHE: THE MECHANISMS AND SIGNIFICANCE OF THE HEADACHE ASSOCIATED WITH BRAIN TUMOR*

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HEADACHE of patients with brain tumor has been considered to be of limited clinical interest. The mechanism of its production has been incompletely understood and its value in localization of the lesion has been minimized. This restriction of interest in the clinical importance of the headache has at least two explanations: first, the location of the pain has seemed to bear little relation to that of the tumor;[1,2,3] and second, tumor headache has been held to be a manifestation of generalized increase in intracranial pressure, and therefore of little value in localization. The observations which have been made regarding the association of headache in certain sites with specific tumor types or locations are few.[4,5,6,7,8,9,10,11] In these, the emphasis is placed upon the occipital headache characteristic of cerebellar tumors and the frontal reference of pain when such lesions produce internal hydrocephalus. The current generally accepted view of the localizing value of brain tumor headache is summarized in two sentences from a text-book of medicine written seventy-three years ago: "Pain in the head [in patients with brain tumor] is frequently limited to a circumscribed space, but the locality may not correspond to the site of the tumor. The pain, however, is generally on the side of the head corresponding to the situation of the tumor and is referred to the occiput if the tumor be situated in or upon the cerebellum."[12]

THE PROBLEM

The purposes of this study were: (1) to define the quality and intensity of brain tumor headache; (2) to ascertain in how many cases the occurrence and location of the headache could be explained and to outline the common mechanisms of brain tumor headache; and (3) to

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define when headache might be expected to have value in diagnosis and localization of brain tumor.

Patient Material

Seventy-two patients with primary brain tumor were selected. Only those patients who made adequate descriptions of symptoms were studied. In all, the location, size and type of tumor were established at operation or autopsy. The tumors were grouped as follow:

Supratentorial tumors:		
Meningioma		15
Glioma		22
Glioblastoma multiforme	13	
Oligodendroglioma	3	
Astrocytoma	2	
Angiosarcoma	2	
Ganglioneuroma	1	
Neuroblastoma	1	
3rd ventricle tumors		2
Hypophysial adenoma		8
Craniopharyngioma		7
		54
Infratentorial tumors:		
Cerebellopontile angle tumors		7
Meningioma	1	
Trigeminal "neuroma"	1	
Acoustic "neuroma"	5	
Cerebellar and fourth ventricle tumors		11
Astrocytoma	5	
Hemangioblastoma	2	
Angiofibroma	1	
Medulloblastoma	1	
Meningeal sarcoma	1	
Glioblastoma multiforme	1	
		18

Headache, either continuous or more frequently intermittent, was present in sixty-five or 9/10, and increased intracranial pressure, in forty-nine or about 7/10 of the patients. The evidence for increased pressure included one or more of the following criteria: papilledema, accentuated convolutional markings on roentgenogram of the skull, ventricular dilatation on ventriculogram, definite manifestations of pressure increase when the ventricles were tapped or the bone flap turned down, and elevated cerebrospinal fluid pressure on lumbar tap.

I. The Quality and Intensity of Brain Tumor Headache

The headache was of a deep, aching, steady, dull nature. It was not rhythmic and seldom throbbing. It was usually intermittent, but in one tenth of the patients it was continuous. The headache was sometimes

severe, but rarely was it as intense as that of migraine or the headache associated with ruptured cerebral aneurysm, meningitis, or certain febrile illnesses or that induced by certain drugs. It was usually relieved by acetylsalicylic acid, or cold packs applied to the scalp, both indications of its moderate intensity. It rarely interfered with sleep. It was aggravated by coughing, or straining at stool and sometimes it was worse in the erect than in the recumbent position. It was commonly aggravated also by the onset of a minor infection. If there were any variation in intensity during the twenty-four cycle, it was worse in the early morning.

Even when the tumor directly compressed or extensively stretched cranial nerves containing pain afferents, the pain was not equal in intensity to that of tic douloureux, and indeed was often mild or absent.[4,6,8,13]

Unless the pain were severe, nausea with tumor headache was slight. Vomiting occurred with displacement or compression of the medulla[14] and was sometimes "projectile," perhaps because it was unexpected when unaccompanied by nausea. The headache when occipital or suboccipital was sometimes associated with "stiffness" or aching of the muscles of the neck and tilting of the head toward the side of the tumor.

II. The Mechanisms of Brain Tumor Headache

Two sets of recent observations on headache mechanisms directly introduce the present study. First of all, data obtained during the operative exposure of intracranial contents have identified those structures which are pain sensitive to mechanical stimulation, and the sites of the headache thus induced.[15,16,17,18] These structures are, in brief, the great venous sinuses and their tributaries from the surface of the brain, the dural arteries, the internal carotid arteries, the cerebral arteries at the base, the basilar and vertebral arteries, the other arteries near their sites of origin from the basilar and vertebral trunks, parts of the dura at the base, and the intracranial portions of the trigeminal, glossopharyngeal, vagus and upper cervical nerves. It was noted, furthermore, that stimulation of the pain sensitive structures on or above the superior surface of the tentorium cerebelli resulted in pain transmitted by the fifth nerve and located in regions on the anterior half of the head.

Stimulation of the pain sensitive intracranial structures on or below the inferior surface of the tentorium cerebelli resulted in pain over the posterior half of the head, the pain pathways being chiefly in the ninth

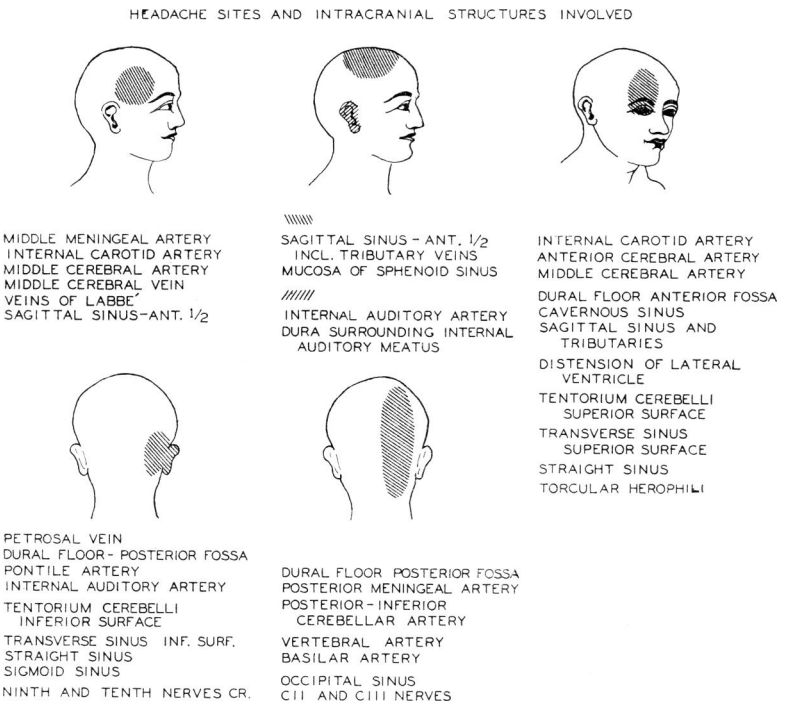

Fig. 1—Summary of intracranial pain sensitive structures which may be the sources of headache in the various main divisions of the head. Chart is based upon data obtained at operative exposure of intracranial contents.

and tenth cranial nerves and the upper three cervical nerves.[18]

These facts of pain reference are illustrated on a chart (Fig. 1) representing the sites of intracranial disease which may account for headache in the various main divisions of the surface of the head.* The chart demonstrates the difficulties inherent in any attempt to use headache as a localizing sign of intracranial disease, since lesions of remotely separated structures within the skull may cause headache in identical areas.

Organization of the data available from these studies has indicated six basic mechanisms of headache, involving distortion or inflammation of intracranial pain sensitive structures.[18]

1. Traction on the large venous sinuses or their tributaries from the surface of the brain.
2. Traction on the middle meningeal artery.

* Eye and paranasal sinus diseases have been eliminated from consideration here. The role of these factors in headache is now being studied.

3. Traction on the large arteries at the base of the brain.
4. Direct pressure upon the cranial and upper cervical nerves which carry pain fibers.
5. Dilatation of intracranial arteries.
6. Inflammation in or about any of the intracranial pain sensitive structures.

It has been suggested that the first four of these six mechanisms may play a part in the headache associated with brain tumor.[18]

A second fact important to an understanding of brain tumor headache is that increased intracranial pressure is not essential to its production.[19] Thus, elevation of the intracranial pressure in normal human subjects to levels as high as 510 mm. of saline by the intrathecal injection of normal saline consistently failed to cause headache. Evidence even more compelling that increased intracranial pressure and tumor headache are not closely related was obtained in the study of a man with ā left parietal oligodendroglioma in whom bifrontal headache had been present intermittently for two months but happened to be absent at the time the following experiment was performed.[19] By drainage of cerebrospinal fluid with the patient horizontal, moderate headache, chiefly left frontal, was induced. The headache was then relieved at once by restoration of fluid and elevation of pressure to its initial level, and furthermore could not be produced by pressure elevation to a high level, 550 mm. of saline. (See also Northfield[10] and Pickering.[20])

1. *Tumor Headache and Increased Intracranial Pressure not Essentially Related:*

In this series of seventy-two patients, the symptom headache occurred almost as commonly in those patients (19 of 23, or about 8/10) without increased intracranial pressure as it did in those (46 of 49, or about 9/10) with increased pressure. Moreover, of the seven patients (about 1/10 of all cases) who were headache-free, three had increased intracranial pressure.

These data demonstrate that increased pressure per se is neither an essential nor a major factor in tumor headache.

2. *Tumor Headache in Patients with Normal Intracranial Pressure—The Mechanism of Local Traction:*

Of the twenty-three patients with normal intracranial pressure, nineteen had headache as a symptom. In all but three patients with hypophysial adenoma, the existence and location of the headache could be

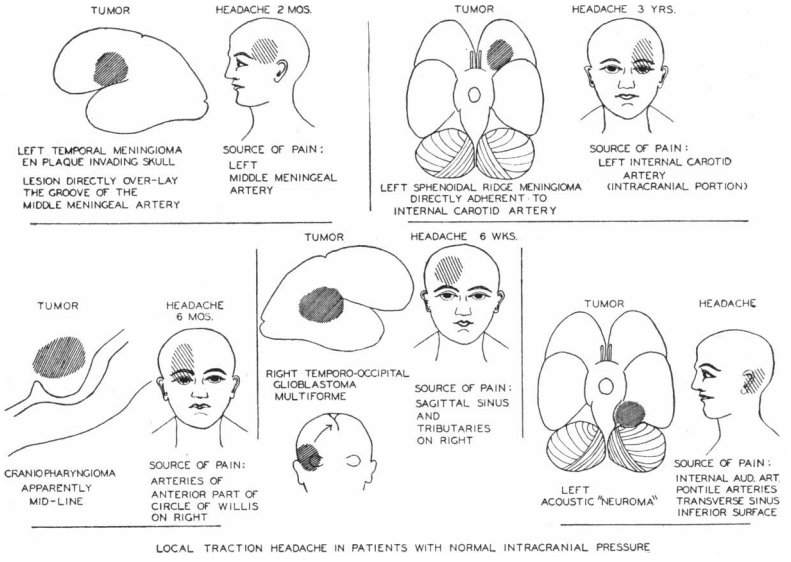

Fig. 2—Five examples of patients with tumor headache produced by local traction. Intracranial pressure was normal in all. The structures which were the probable sources of the pain are listed in each case.

explained by traction upon or distortion of directly neighboring pain sensitive structures, and in some at operation the headache was thus reproduced. These adjacent structures were: (1) for the four supratentorial meningiomas—the superior sagittal sinus and its tributaries, the middle meningeal artery and the large arteries at the base; (2) for the one glioma—the superior sagittal sinus and its tributaries; (3) for the three craniopharyngiomas—the large arteries at the base; (4) for the four hypophysial adenomas—the large arteries at the base and in one patient the lining of the sphenoid sinus; and (5) for the four cerebellopontile angle tumors—the internal auditory artery, the pontile arteries, the dura about the internal auditory meatus, and the transverse sinus. In Fig. 2 are shown examples of this group.

Another example of the headache produced by local traction may be cited (Fig. 3). A thirty-seven year old male with a trigeminal "neuroma" in the right cerebellopontile angle and no evidence of increased intracranial pressure had had for four months three separate kinds of head discomfort. These, with the sites of origin of the symptoms, were: (1) right temporal "tightness"—fifth cranial nerve; (2) "soreness" in the

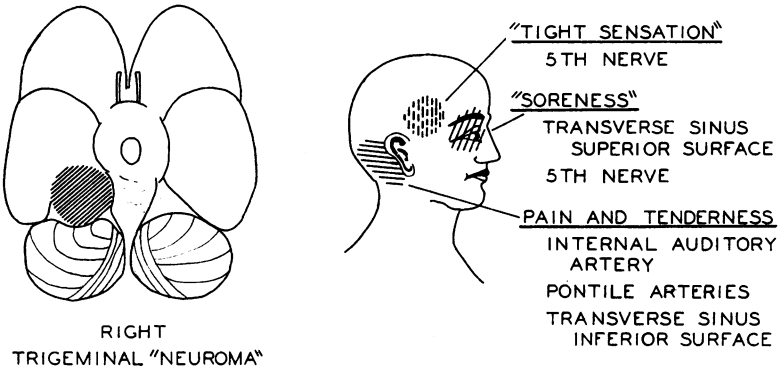

Fig. 3—Demonstration of local traction headache mechanisms in an adult male with three separate types of head discomfort, due to a trigeminal "neuroma" in the right cerebellopontile angle. The intracranial pressure was normal.

right eyeball, superior surface of the right transverse sinus and fifth cranial nerve; (3) pain and tenderness in the right postauricular area, right internal auditory and pontile arteries and inferior surface of the transverse sinus.

This mechanism of tumor headache may be termed local traction. While independent of increase in intracranial pressure, it may well be augmented by generalized displacement of the brain associated with cerebrospinal fluid pressure rise.

The three patients with hypophysial adenoma in whom local traction did not entirely account for the headache had pain in the occiput or subocciput in addition to frontotemporal headache. The pain in the back of the head in these three of the seven patients with hypophysial adenoma is unexplained.

3. *Tumor Headache in Patients with Increased Intracranial Pressure —The Mechanisms of Local and Distant Traction:*

In less than one-half (18) of those patients (46) with headache and increased intracranial pressure could the locations of the headache be explained or the pain induced by local traction. Most of the remaining half of the patients had posterior head pain in association with supratentorial tumors and frontal headache in association with infratentorial

tumors. The following analysis of the group illuminates this seeming paradox.

A. DISTANT TRACTION THROUGH EXTENSIVE DISPLACEMENT OF THE BRAIN:

Slightly less than one-half (14 of 32) of the patients with supratentorial tumor with headache had pain in the posterior half of the head—occipital, suboccipital or postauricular areas. In seven patients this pain was bilateral. In the seven in whom it was unilateral it was homolateral to the tumor in all but one. In each instance pain was also present in one or several other head regions.

Headache so located in these patients could not be explained by local traction, for there is no evidence that any supratentorial structure can be the direct source of posterior head pain. Pressure downward upon the tentorium cerebelli from above has been shown experimentally to cause only fronto-orbital pain,[18] probably by traction upon the upper surfaces of the transverse sinuses. Such a mechanism, therefore, cannot be relevant to posterior head pain. It has been recognized, however, that when supratentorial lesions are large enough to cause generalized increase in pressure, there is often a widespread shift in the brain causing distortion of supra- and infratentorial structures. Thus, traction or pressure upon the transverse and occipital sinuses, the basilar and vertebral arteries, the ninth and tenth cranial and upper cervical nerves is probably a common occurrence. However, with supratentorial tumor the extent of such distortion in the posterior fossa is much less and the establishment of a "cerebellar pressure cone" is less likely than in patients with infratentorial tumor.

Herniation of the hippocampal gyri through the incisura tentorii may also be responsible for posterior head pain from supratentorial tumors. In a recent review of autopsied cases of supratentorial neoplasms such a complication was found in about 8/10 of the series.[21] The distortion produced by this "temporal pressure cone" has been shown to affect not only the hippocampal gyri but also the adjacent brain stem, and presumably the basilar artery and its branches. This mechanism must be considered to be of minor importance as regards the present problem, for in the autopsied series reported, posterior head pain was no more common in the patients with such herniation than in those without it.

In brief, posterior head pain in patients with supratentorial tumor appears to depend upon expansion of the mass to such an extent that

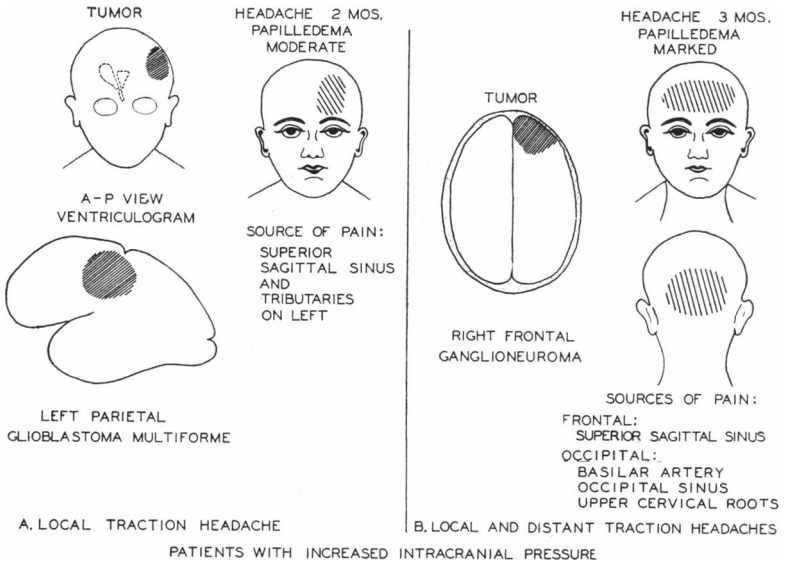

Fig. 4—Local and distant traction mechanisms in tumor headache contrasted in two patients with increased intracranial pressure. In A the headache was due to local traction alone; in B the frontal headache was due to local traction, the occipital headache to distant traction.

coincident with generalized rise in intracranial pressure, traction is produced upon pain sensitive structures in the distant posterior fossa, by displacement of the whole brain. In contrast to local traction this may be conveniently termed distant traction and may be considered as a second mechanism of brain tumor headache. It is evident that in extensive shift of the brain, traction effected at a distance from the tumor may involve structures on the same side as the tumor or both sides. The data indicate that both situations are common.

Two cases of supratentorial tumor with increased pressure are illustrated in Fig. 4A and B. In A, a patient with a left parietal glioblastoma multiforme and moderate papilledema, the left frontal headache was due to traction locally by the mass upon the superior sagittal sinus and its tributaries on the left. The ventriculogram is reproduced in outline to emphasize the type of distortion which was present. In B, a patient with a right frontal ganglioneuroma and advanced papilledema, the frontal headache was similar in its mechanism to that of A. The occipital headache represented distant traction upon structures in the posterior fossa, secondary to widespread displacement of the brain.

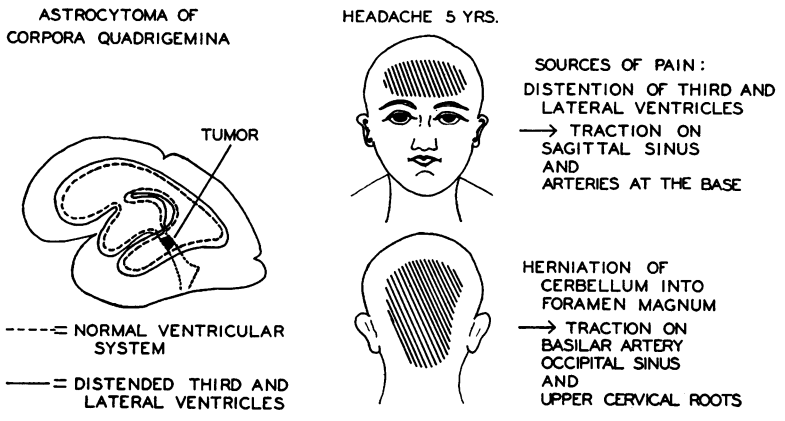

Fig. 5—Demonstration of distant traction headache produced by a small astrocytoma in the roof of the aqueduct. The frontal headache was due to internal hydrocephalus, the occipital headache to distortion of posterior fossa structures by wedging of the cerebellum into the foramen magnum.

B. DISTANT TRACTION THROUGH INTERNAL HYDROCEPHALUS:

Frontal headache was a symptom in two-thirds (10 of 14) of the patients with infratentorial tumor and increased intracranial pressure, all of whom had headache. This fact likewise required explanation in terms other than local traction by the tumor. Analysis revealed that 9 of the 10 with frontal headache, comprising 2 angle tumors and 7 cerebellar or fourth ventricle tumors, were complicated by block to the cerebrospinal fluid outflow at the aqueduct or the fourth ventricle and had internal hydrocephalus with increase in intracranial pressure. The frontal headache was bilateral in all but one patient.

The association of internal hydrocephalus with frontal headache in patients with infratentorial tumor has been noted by others.[5, 8] Direct evidence that the hydrocephalus is causally related to the headache has been provided by the demonstration that distention of one lateral ventricle with a balloon at operation induces homolateral frontal headache[18] by traction upon the veins over the convexity of the brain anchoring it to the superior sagittal sinus. Experimental distention of the third ventricle has been found to cause diffuse headache arising from traction upon the many large vessels at the base. There is further evidence that

significant distortion of adjacent structure at the base is produced by enlargement of the third ventricle in internal hydrocephalus, for in such patients a visual field defect indicative of chiasmal pressure has often been found.[22] The usual bilaterality of the frontal headache in these patients may therefore be understood.

Hence, frontal headache of this kind is like the posterior head pain discussed in the previous section in that it is produced by traction at a distance from the tumor.

An example of a small tumor producing headache entirely by distant traction is outlined in Fig. 5. A sixteen year old male had intermittent bifrontal and bioccipital headache for five years. On admission moderate papilledema was noted. The ventriculograms showed advanced dilatation of the third and lateral ventricles. Exploration confirmed the presence of internal hydrocephalus. The foramina of Monroe were widely stretched, the largest diameter of the left opening measuring 2.5 cm. Moreover, as seen in a second exploration, the tonsils of the cerebellum were herniated in part into the foramen magnum. No tumor could be found, but autopsy revealed a small fibrillary astrocytoma of the corpora quadrigemina occluding the aqueduct of Sylvius. The frontal headache was due to distention of the lateral, and possibly the third, ventricles. The occipital headache was due to traction upon the basilar artery, the occipital sinus, the ninth and tenth cranial nerves and upper cervical roots by the wedging of the cerebellum down into the foramen magnum. The site of origin and the location of both frontal and occipital headaches were remote from the tumor itself.

C. TUMOR HEADACHE UNEXPLAINED BY LOCAL OR DISTANT TRACTION:

In two patients with increased intracranial pressure the headache could not clearly be related to these mechanisms. One, a twenty-four year old female, had a left temporal headache for five months. She had a right acoustic "neuroma," increased intracranial pressure and internal hydrocephalus.

The other, a forty-four year old female, had right occipital headache for six months. She had a left cerebellar hemangioblastoma, increased intracranial pressure and internal hydrocephalus.

Headache in this pattern, sparing the homolateral side but involving the contralateral side, appears bizarre. The direction and distribution of the stress and strain in these two cases is conjectural and the factors

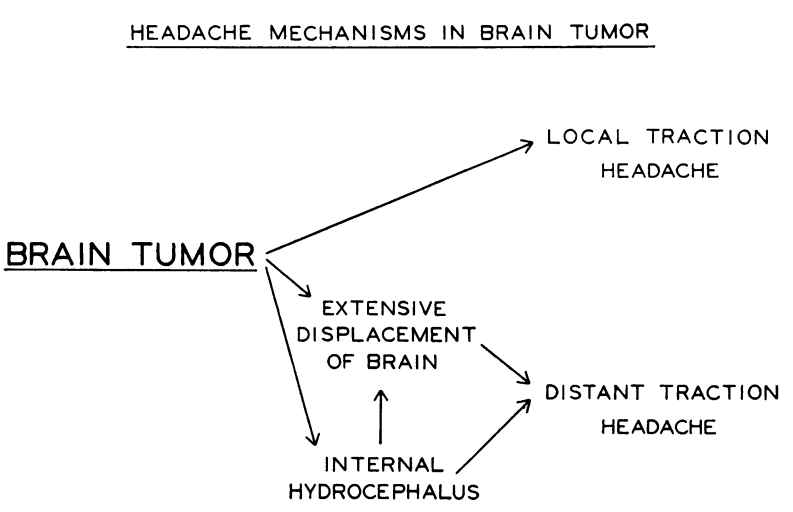

Fig. 6—Schematic outline summarizing common mechanisms of brain tumor headache.

which make them atypical are not apparent. There is no evidence, however, that mechanisms other than traction upon pain sensitive structures are involved.

Thus, in forty-four of the forty-six patients with headache and increased intracranial pressure the existence and location of the headache could be accounted for on the basis of the mechanisms thus far outlined. In many (18) local traction alone appeared to be responsible. In a few (4) traction at a distance alone was responsible, either through displacement of posterior fossa structures in patients with supratentorial tumors or through internal hydrocephalus in patients with infratentorial tumors, but, in the largest group (22) both local and distant traction were concerned. In 2 patients the headache could not be clearly explained by either mechanism.

It is to be emphasized that the association of increased intracranial pressure with headache due to distant traction does not justify the inference that increased intracranial pressure of itself causes headache. It indicates rather that the same factors which bring about distant traction, that is, extensive displacement of the brain directly by the tumor or indirectly by internal hydrocephalus, will also cause generalized elevation of intracranial pressure. (See Fig. 6.)

4. Continuous vs. Intermittent Headache with Brain Tumor:

As mentioned above, the headache of brain tumor is usually inter-

mittent. In this series continuous headache was noted in only seven cases or about a tenth of the patients (all with supratentorial tumor). Four of these had increased intracranial pressure. Local traction appeared to be the mechanism in all seven cases. The persistence of the headache in these cases is not surprising, for it is reasonable to expect local traction to be continuous, and in fact progressive, if the tumor growth is moderately rapid. There is no explanation of the intermittency of the headache that will apply to all the remaining large group of patients. In some, intermittent block to cerebrospinal fluid outflow either because of varying states of brain hydration or by movable tumors in the 4th or 3rd ventricles appears to have been responsible. In others the increase in intracranial venous pressure with straining and coughing might have been the basis for occasional headache.

5. Patients with Brain Tumor without Headache:

Seven patients, or about a tenth of the entire series, had no headache in association with their lesions. The tumors represented were all supratentorial; in three of the seven increased intracranial pressure was present.

Associated with increased intracranial pressure and without headaches were:

Tumor Type	*Site*
Meningioma	left parasagittal parietal
Glioblastoma multiforme	right frontocallosal
Glioblastoma multiforme	left frontal (subcortical)

Associated with normal intracranial pressure and without headaches were:

Tumor Type	*Site*
Meningioma	right frontotemporal (invading the skull)
Oligodendroglioma	left frontotemporal
Oligodendroglioma	right temporoparietal
Craniopharyngioma	suprasellar (sella and dorsum destroyed)

Review of these patients disclosed that the only characteristic common to all was a supratentorial location of the tumor.

The absence of headache in patients with brain tumor may be related to the slow growth of the neoplasm. Thus five of the above seven patients had lesions which are notably slow in expanding, i.e., meningioma, craniopharyngioma and oligodendroglioma. Moreover, in one of the two patients who were headache-free with glioblastoma multiforme, ordinarily a rapidly growing neoplasm, the clinical course indicated unusually slow growth of the tumor. When expansion of the tumor mass is slow, mechanical adaptation of adjacent structures may be sufficient to

prevent pain production. This may represent the return of distorted pain endings to normal contour even though gross distortion of the tissues in which the pain endings are embedded persists. When the pace of growth is fast, such adaptation may be inadequate.[6, 13]

It may be noted that in contrast to tumors above the tentorium, posterior fossa tumors, whatever their rate of growth, rarely fail to cause headache, undoubtedly because many of these lesions cause internal hydrocephalus.[5, 8] In consideration of headache the speed of growth of the posterior fossa tumor is less significant since it bears no direct relation to the completeness of occlusion of the iter or the fourth ventricle. A block once induced results in a relatively sudden displacement of the brain and stimulation of local and distant pain sensitive structures.

Serious sensorial defects produced by the tumor, particularly with frontal lobe lesions, may be a second cause for absence of headache. For example, in the second of the two patients with glioblastoma multiforme without headache, listed in the table above, the tumor was in the right frontocallosal region and apathy and confusion were early and dramatic symptoms. Under such circumstances, gross defects in reaction to pain may veil or completely mask headache.

Invasion of the skull by meningiomas may be still a third factor in preventing or delaying headache. The bone of the skull is insensitive and extension in this direction may take the place of greater intracranial expansion toward pain sensitive structures.

6. Consideration of Other Suggested Mechanisms.

In these formulations distortion of pain sensitive structures has been described as the chief basis for brain tumor headache. Factors other than traction have been suggested by others but not established as relevant mechanisms. Dilatation of intracranial veins and arteries, which occurs secondary to generalized increase in intracranial pressure, may conceivably be a cause of headache.[10, 18] Such vasodilatation must, however, be of minor importance as a cause of headache in patients with tumor since it has been shown in this discussion that increased intracranial pressure is not essential to the headache, and the pain in these patients is usually localized rather than diffusely distributed as it should be if generalized dilatation of intracranial vessels were the cause. Stretch of the dura mater over the convexities of the cerebrum and cerebellum by the rise in intracranial pressure is also probably not a significant mechanism, because the dura and pia in these areas are insensitive.

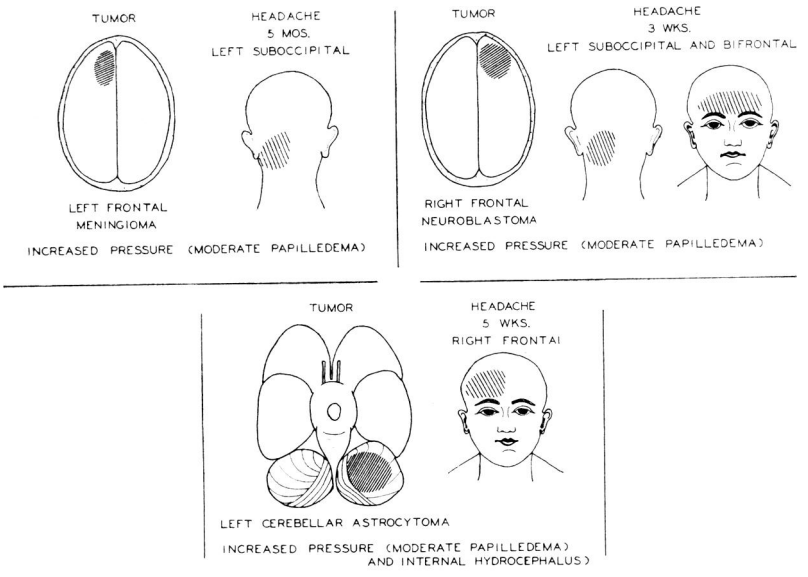

Fig. 7—Demonstration of headache as a grossly misleading sign of the location of brain tumor when it is due to distant traction. Extensive displacement of the brain and increased intracranial pressure were present in all three patients.

III. Headache in the Localization of Brain Tumor

A. Limitations of Headache as a Localizing Sign:

1. Headache in Association with Increased Intracranial Pressure of Limited Localizing Value:

In the preceding section it was noted that headache in patients with normal intracranial pressure could, with rare exceptions, be explained entirely in terms of local traction. Of patients with increased intracranial pressure in only eighteen of forty-six, or about 4/10, was local traction solely responsible; in the remaining twenty-six distant traction was an accessory or the chief mechanism.

When distant traction is involved the problem of localization of the tumor is complicated, for with this mechanism distortion of bilateral pain sensitive structures is common, and the site of the expanding mass is often concealed. It is evident, therefore, that in the presence of increased intracranial pressure, which in patients with brain tumor is

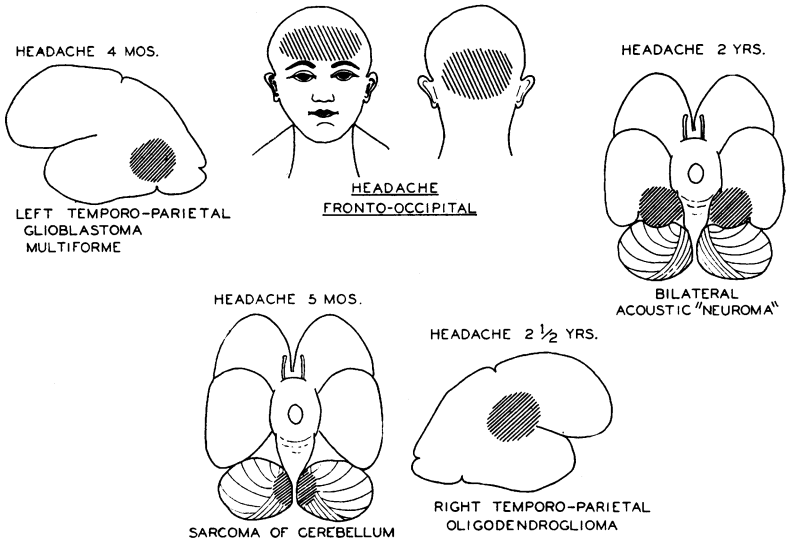

Fig. 8—Demonstration of fronto-occipital headache occurring with tumors of widely varying types and locations and therefore of no localizing value. Extensive displacement of the brain and increased intracranial pressure were present in all.

presumptive evidence of extensive displacement of the brain, the localizing value of tumor headache becomes reduced. Examples of patients with headache as a misleading sign when secondary to distant traction are shown in Fig. 7.

2. Fronto-occipital Headache of No Localizing Value:

The combination of frontal and occipital headache was noted in one-quarter of all the patients with headache. The group with fronto-occipital headache included patients with meningioma, cerebral glioma, third ventricle cyst, hypophysial adenoma, cerebellopontile angle and cerebellar and fourth ventricle tumors. Except for the two instances of hypophysial adenomas, all were accompanied by increased intracranial pressure. Internal hydrocephalus was present with only one of the supratentorial tumors, the 3rd ventricle cyst, but was present with all five infratentorial tumors.

The data indicated that fronto-occipital headache occurred almost as frequently with supratentorial tumors as with those below the ten-

torium. Moreover, they showed conclusively that the fronto-occipital headache combination cannot be considered diagnostic of internal hydrocephalus in patients with brain tumor. It is of additional interest that except for the hypophysial adenomas all of the patients with headache of this pattern had increased intracranial pressure.

Four typical instances of brain tumor of contrasting types and location, all presenting fronto-occipital headache, are outlined in Fig. 8.

3. Headache Over the Vertex—Infrequent and of Little Localizing Value:

Headache over the vertex was noted infrequently in this series. In only three patients was the headache in the vertex alone; these were a mid-line olfactory groove meningioma, a craniopharyngioma and an eosinophilic hypophysial adenoma. In the first two the intracranial pressure was elevated. In two other patients headache was vertical in part but not predominantly; the tumors found were a parasagittal parietal meningioma and a mid-line cerebellar astrocytoma, both with increased pressure.

4. Headache from Mid-line Tumors Not Always Bilateral:

Twenty-three mid-line tumors with headache were included in this series. In seventeen patients the headache was symmetrically bilateral, eleven having increased intracranial pressure. In six the headache was entirely or predominantly unilateral; none of these had increased intracranial pressure.

Local traction apparently was the mechanism for the headache when it was unilateral. The inequality of the distortion produced may have been due to unrecognized asymmetrical expansion of the growing tumor. Whatever the explanation, it is clear that unilateral headache may occur with mid-line tumors.

B. THE ASSETS OF HEADACHE AS A LOCALIZING SIGN:

The limitations of headache having thus been considered, its value may now be appraised.

1. Headache Near or Overlying the Tumor:

Headache to be of service as a localizing sign of brain tumor must be interpreted in terms of the headache mechanisms and principles of pain reference just outlined. Only when tumor headache is caused solely by local traction is it of direct value in localization. Even then the headache may not overly the tumor, for in about 4/10 of the patients with

headache due only to local traction the pain was not immediately over the tumor. In the following analysis certain tumors located at the base and anteriorly were not included since obviously they could not produce headache near to or directly overlying the tumor, other than in the nasopharynx. These lesions were the craniopharyngiomas, hypophysial adenomas, a suprasellar meningioma, and a third ventricle cyst. The evidence in summary, based on the remaining 22 patients with local traction headache, was as follows:

	Headache was near to or overlying the Tumor
Supratentorial Tumors	
Meningioma	3 of 6
Glioma	4 of 9
Infratentorial Tumors	
Cerebellopontile angle tumors	4 of 4
Cerebellar and 4th ventricle tumors	2 of 3
	13 of 22

When the analysis was broadened to include all the patients (again excluding the tumors at the base) headache was found to overly the tumor in only nineteen of fifty-one, or about one-third.

2. Headache as First Symptom of Brain Tumor:

With the exception of the cerebellopontile angle tumors, the presence of most of the posterior fossa tumors first was made manifest by headache. The tumors above the tentorium, on the other hand, were more likely first to cause other symptoms, as visual disturbances, paresthesias, convulsions, sensorial and personality changes. Other authors have reported similar observations.[3, 6, 10] Northfield's figures[10] based upon a series of 100 cases are presented in brackets for comparison with the data of this New York Hospital series. Headache as first symptom of brain tumor:

		Northfield[10]
In 54 cases of supratentorial tumor		
Meningioma	5 of 15	[36 per cent]
Glioma	11 of 22	[36 per cent]
3rd ventricle tumors	1 of 2	
Hypophysial adenoma	1 of 8	
Craniopharyngioma	2 of 7	
	20 of 54 or about one-third	
In 18 cases of infratentorial tumor		
Cerebellopontile angle tumors	1 of 7	[0]
Cerebellar and 4th ventricle tumors	9 of 11	[83 per cent]
	10 of 18	

The usual occurrence of headache as first symptom in patients with cerebellar or fourth ventricle tumors is related to the fact that internal

hydrocephalus can easily result from such lesions. Angle tumors, however, are less frequently associated with internal hydrocephalus in the early stages and are directly adjacent to the several cranial nerves which traverse the angle region, potential sources of such symptoms as facial paresthesias, deafness, tinnitus, or weakness of face or jaw. Whether or not supratentorial tumors cause focal symptoms or signs before headache appears, depends upon the region of the brain involved.

3. *The Significance of Headache in the Back of the Head and Neck with Brain Tumor:*

Pain in the back of the head—occipital, or postauricular or suboccipital areas—was present alone or in part in one-half of the patients.* As described in a preceding section, such pain was present in seventeen of the forty-seven patients with supratentorial tumor with headache. In each of these, headache was present also in one or several other areas on the anterior half of the head. Except for the patients with hypophysial adenoma, headache in all was accompanied by increased intracranial pressure.

In contrast, pain in the back of the head was present in almost all of the patients with infratentorial tumor. Of the eighteen patients sixteen or almost 9/10 had posterior headache. The two without such headache had respectively an acoustic "neuroma" and a cerebellar astrocytoma, both accompanied by increased intracranial pressure.

It seems generally true, therefore, that occipital, suboccipital or postauricular pain did not of itself identify a tumor as being above or below the tentorium. On the other hand, the evidence did indicate that when posterior headache was absent the tumor was rarely infratentorial.

4. *The Significance of Headache in the Front of the Head with Brain Tumor:*

Frontal headache with brain tumor in this series was even more common than was pain in the back of the head. In 6/10 of all patients with headache, frontal headache was present, alone or with headaches elsewhere. In contrast to pain in or near the occiput, frontal headache was noted somewhat more often in association with supratentorial tumors (32 of the 47 with headache or about 7/10) than with infratentorial tumors (10 of 18 or about one-half).

Pain solely frontal was noted in eleven of the forty-seven cases of supratentorial tumor with headache but in only two of the eighteen

* For the sake of brevity pain of this type will be referred to hereafter as posterior headache.

cases with infratentorial tumor or headache.

The predominance of frontal headache is not surprising in view of the diverse ways, direct and indirect, in which brain tumor may produce pain referred to the frontal areas. But from the data it may be inferred that although frontal headache was common in all types and locations of tumor, the pain when solely frontal was usually due to supratentorial tumor.

5. The Significance of Unilateral Headache:

It has been shown above that mid-line tumors may cause unilateral headache, probably because of asymmetrical expansion of the mass. Further data concerning the significance of unilateral headache were derived from an analysis of the forty-two remaining patients with headache and tumor not in the mid-line. The headache patterns were as follows:

Headache homolateral to the tumor	24
Headache contralateral to the tumor	5
Headache symmetrically bilateral	13

All five patients with headache contralateral to the tumor had increased intracranial pressure. In three of these five the contralaterality of the headache was the result of distant traction.

It is evident that headache chiefly on one side of the head was common in these patients, and that in most cases the headache was on the same side as the tumor (See also Pickering[20]). Contralateral headache may have resulted from the presence of anatomical asymmetries in the brain or skull such as the size or position of the lateral or third ventricles, or the relative position of the cerebellum, brain stem and anchoring structures in the posterior fossa. In none of the patients with normal intracranial pressure was contralateral headache noted. The important inference from these considerations is that headache solely or chiefly unilateral is probably on the same side as the tumor when the intracranial pressure is normal.

C. VARIOUS TYPES OF TUMORS IN RELATION TO HEADACHE:

Among patients with craniopharyngiomas, headache as an initial symptom was rare and its location unpredictable. The hypophysial adenomas also rarely produced headache as an initial symptom, and the site of the headache presented nothing of specific or helpful value.

Among most of the patients with headache due to cerebellopontile angle tumors the headache was a leading clue in the localization of the

lesion, although headache did not occur as an early symptom. Headache solely in the postauricular area was almost specific, especially before gross displacement of the brain occurred.

Among patients with meningiomas (all but one being supratentorial), headache was a first symptom in one-third. In about one-half of the fourteen patients with headache the headache was predominantly unilateral and on the same side as the tumor, and in all but two of the fourteen cases the headache was due to local traction. It might be expected that situated as the meningiomas are, in contact with pain sensitive structures at the base and over the convexities, that headache as an initial symptom might occur in a higher proportion than the one-third indicated. It is probable, however, that the slow growth and bone invasion offset the effects of proximity to pain sensitive vascular structures.

Gliomas, despite their lack of direct contact with pain sensitive structures, presented headache as a first symptom in one-half of the patients when they occurred above the tentorium and even more frequently when they occurred below. Such tumors produced headaches as an early manifestation probably because of their speed of growth and the likelihood of their occluding the lateral, third, and fourth ventricles.

D. GENERALIZATION:

From these studies the following generalizations concerning brain tumor headache as an aid to localization seem justified.

1. Although the headache of brain tumor is often referred from a distant intracranial source, it approximately overlies the tumor in about one-third of all patients.

2. Brain tumor headache in the absence of papilledema is of great localizing value. In about two-thirds of such patients the headache immediately overlies or is near the tumor and in all when unilateral it is on the same side as the tumor.

3. Headache is almost always present with posterior fossa tumor.

4. Headache may be absent with any of the common types of supratentorial tumor.

5. The headache of posterior fossa tumor is almost always over the back of the head, although it may occur elsewhere as well.

6. Headache is usually the first symptom of posterior fossa tumor except with cerebellopontile angle tumors.

7. Headache is the first symptom of one-third of supratentorial tumors.

8. The headache of cerebellopontile angle tumors is frequently and sometimes solely postauricular.

9. Headache from supratentorial tumors is rarely in the back of the head unless associated with papilledema.

10. When supratentorial tumors cause headache in the back of the head, headache in the front of the head is usually also present.

11. When headache is both frontal and occipital it indicates extensive displacement of the brain and has little localizing value.

12. Brain tumor headache is commonly intermittent but when it is continuous its value in localization is greatly enhanced.

Conclusions

1. Brain tumor headache is produced by traction upon intracranial pain sensitive structures, chiefly the large arteries, veins and venous sinuses, and certain cranial nerves. There are two types of traction which operate singly or in combination: local traction by the tumor mass upon adjacent structures; and distant traction by extensive displacement of the brain, either directly by the tumor or indirectly by ventricular obstruction (internal hydrocephalus).

2. As an aid in the localization of brain tumor, the value of headache is limited by two facts: the headache may be remote from the site of its production, and the site of production of the headache may be remote from the tumor.

3. In spite of these limitations, when it is interpreted in terms of known principles of intracranial pain production and pain reference, the headache of brain tumor may aid significantly in the diagnosis and localization of the lesion.

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* We wish to acknowledge the help of Miss Helen Goodell in the preparation of the manuscript and the illustrations.

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